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Surgical treatment and prognosis of octogenarians with non-small cell lung cancer

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ABSTRACT

Objective: To explore the clinical characteristics, surgical treatment and prognosis of non-small cell lung cancer (NSCLC) among elderly patients over 80 years. **Methods:** The clinical data, surgical methods, perioperative management, postoperative complications and prognosis of 52 NSCLC patients aged over 80 years were retrospectively analyzed. **Results:** Out of 52 cases, 27 had a long-term smoking history (51.9%) and 44 were with other diseases (84.6%). Lobectomy was done in 32 cases (65.4%), sub-lobectomy in 20 cases (38.5%), including pulmonary wedge resection in 16 cases (30.8%) and lung segment resection in 4 cases (7.7%). The postoperative complication rate was 44.2% (23/52); the complication rate after lobectomy was 62.5% (20/32) and that after sub-lobectomy was 25% (5/20), with significant difference between lobectomy and sub-lobectomy ($P < 0.05$). Postoperative mortality was 3.8% (2/52). Pathological TNM staging: I a 27 cases (51.9%), I b 12 cases (23.1%), II a 8 cases (15.4%), II b 3 cases (5.8%) and III a 2 cases (3.8%). The 1-, 3- and 5-year survival rate after operation was 87.1%, 59.8%, 19.1%. The 1-, 3- and 5-year survival rate was 86.0%, 61.8%, 21.5% in the patients after lobectomy; that was 89.0%, 58.3%, 18.7% in the patients after sub-lobectomy, with no significant difference between two surgical methods ($P > 0.05$). **Conclusions:** Octogenarians with NSCLC are often afflicted with comorbidity, so perioperative management is more complex. Strictly adhering to indications, surgery is still an important treatment of NSCLC patients over 80.

1. Introduction

With social progression and global aging, more elderly are affected by lung cancer and their morbidity and mortality present a significant increase. Surgery is an important treatment method for non-small cell lung cancer (NSCLC). However, because of degraded physiological function, variety of comorbidities, high risk of complications during operation and mortality among elderly patients^[1], doctors as well as patients tend to give up surgery in consideration of age, especially when dealing with NSCLC patients aged over 80. This is one reason why elderly NSCLC patients can not be effectively treated. During January 1998 and December 2011, 52 NSCLC patients over 80 years were admitted to our

hospital and treated, hereby we summarized their clinical features, surgical methods, perioperative management and prognosis as follows.

2. Materials and methods

2.1. Clinical data

Totally 52 patients, 39 males and 13 females, aged 80–90 years with mean age of 83.6 were selected. Preoperative examinations included routine blood test, liver and kidney function, chest X-ray, electrocardiogram, ultrasound echocardiography, abdominal B ultrasound, pulmonary function, cranial CT or MRI, chest and abdominal CT, whole body bone scan; some patients underwent fiberoptic bronchoscopy, CT-guided puncture or PET-CT examination. A clear preoperative diagnosis was made and

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distant metastases were excluded. Lesions located in left upper lobe in 8 cases, left lower lobe in 4 cases, right upper lobe in 23 cases, right middle lobe in 3 cases, right lower lobe in 14 cases.

Preoperative abnormal ECG was found in 29 cases (55.8%), including abnormal ST in 21 cases, bundle branch block in 9 cases, premature ventricular contractions in 5 cases, and atrial fibrillation in 3 cases. Twelve cases were found 1 second forced expiratory volume or maximum voluntary ventilation <60% in pulmonary function test. Among all patients, 19 cases (36.5%) were found with one comorbidity, 21 cases (42.3%) with two comorbidities, 4 cases (7.7%) with three and 8 cases (15.4%) without. The patients were accompanied with hypertension in 27 cases (51.9%), coronary heart disease in 19 cases (36.5%), chronic obstructive pulmonary disease (COPD) in 7 cases (13.5%), diabetes in 5 cases (9.6%), cerebral infarction in 2 cases (3.8%), postoperation for removal of gastric cancer in 1 case (1.9%), chronic nephritis in 1 case (1.9%). Twenty-seven cases (51.9%) had smoking history. Clinical symptoms included chronic cough in 16 cases (30.8%) [9 cases were found blood stained sputum (17.3%)], chest pain in 6 cases (11.5%), other discomfort in 10 cases (19.2%), and 20 cases (38.4%) discovered in physical examination.

2.2. Perioperative management

Once admitted, all patients were dealt with their accompanying diseases, and their blood pressure was controlled between 120–140/70–90 mmHg; to those with coronary heart disease, vasodilator and myocardial nutritional medicine were given and aspirin was discontinued one week before operation; To those with arrhythmia, antiarrhythmic drugs were applied to restore sinus rhythm; Smokers were required to quit, and no smoking for at least 2 weeks before operation; To those who coughed and expectorated a lot, aerosol inhalation was given, and sputum culture and drug susceptibility test were conducted and antibiotics was used 3 days before operation. After operation, the monitoring of breathing, blood pressure, heart rate, blood oxygen saturation should be carried out for more than three days, and antibiotics was used to prevent infection, aerosol inhalation was used to assist coughing and expectoration, nutritional support should be strengthened and the water and electrolyte balance should be maintained. Special attention should be paid to preoperative accompanying diseases, such as nourishing cardiac muscle and dilating coronary artery, so as to manage them effectively and timely.

2.3. Surgical methods

Double-lumen endotracheal intubation was adopted in

general intravenous anesthesia, and the contralateral lung was for ventilation. Anatomic lobectomy and lymph node dissection was done in 32 cases (65.4%), in which the left upper lobe resection was done in 5 cases, left lower lobe resection in 3 cases, right upper lobe resection in 15 cases, right middle lobe resection in 2 cases, and right lower lobe resection in 7 cases. Sub-lobectomy and systematic lymph node sampling was conducted in 20 cases (38.5%), including pulmonary wedge resection in 16 cases (30.8%) and lung segment resection in 4 cases (7.7%). The operation time ranged 45–210 min with an average of 120.00±56.94. Blood loss during operation was 50–300 mL with an average 174.40±54.97.

2.4. Statistical methods

SPSS software was applied. The enumeration data were processed by using χ^2 test; Survival rate by Kaplan–Meier method and log-rank test. $P<0.05$ was referred to as statistically significant difference.

3. Results

3.1. Pathologic results after operation

The pathological types verified after operation: squamous cell carcinoma in 19 cases (36.5%), adenocarcinoma and bronchioloalveolar carcinoma in 10 cases (19.2%), pure bronchioloalveolar carcinoma in 9 cases (17.3%), adenocarcinoma in 8 cases (15.4%), adenosquamous carcinoma in 4 cases (7.7%), squamous cell carcinoma and large cell carcinoma in 2 cases (3.8%). Postoperative pathologic TNM staging: I a 27 cases (51.9%), I b 12 cases (23.1%), II a 8 cases (15.4%), II b 3 cases (5.8%), III a 2 cases (3.8%).

3.2. Postoperative outcomes

Postoperative complications occurred in 23 cases (44.2%). Arrhythmia happened in 15 cases (28.9%), including sinus tachycardia in 10 cases (19.2%), atrial fibrillation in 8 cases (15.4%), premature ventricular contractions in 4 cases (7.7%); lung infection in 4 cases (7.7%) with one case of respiratory failure; atelectasis in 3 cases (5.8%); persistent air leak lung more than one week in 2 cases (3.8%); acute heart failure in 2 cases (3.8%); acute cerebral infarction in 1 case (1.9%); acute myocardial infarction cases (1.9%). Perioperative death occurred in 2 cases (3.8%), respectively due to acute myocardial infarction and respiratory failure caused by severe lung infection. The complication rate after lobectomy was 56.3% (18/32), while that after sub-lobectomy was 25.0% (5/20), with significant difference ($P<0.05$).

3.3. Follow-up results

All 52 patients were followed up until December 2011. The follow-up rate was 94.2%, with 3 lost cases. The postoperative 1-, 3- and 5-year survival rate was 87.1%, 59.8% and 19.1%. The postoperative 1-, 3- and 5-year survival rate was 86.0%, 61.8% and 21.5% among the patients after lobectomy and was 89.0%, 58.3%, 18.7% among the patients undertaking sub-lobectomy, without significant difference ($P>0.05$).

4. Discussion

Lung cancer is a malignant tumor of global highest morbidity and mortality, in which NSCLC accounts for about 80%–85%. Lung cancer is a typical age-related disease. The median age of lung cancer has reached 71 years in the United States[2]. China has gradually entered the aging society, and the incidence of lung cancer has kept increasing in the elderly. Organs decrease significantly in their functions after one enters into his/her seventies. Currently NSCLC happened in those over 70 is defined as elderly NSCLC domestically and abroad[2]. The super-aged (over 80) patients with lung cancer account for 7.5%–14% of total lung cancer patients[3,4]. However, there are no standard treatment options and corresponding guidelines specific for these elderly patients.

Most of elderly NSCLC patients have a long smoking history associated with chronic bronchitis, which is likely to lead to overlook of respiratory symptoms and delay in treatment. Therefore, the appearance of symptoms like chronic cough or abnormal cough, sputum stained with blood, might indicate lung cancer and necessary checks should be conducted. Out of 52 cases of elderly NSCLC in our study, 32 cases (61.6%) presented clinical symptoms, mainly cough, sputum stained with blood; another 20 cases (38.4%) were discovered by means of physical examination. The patients found by physical examination were at early stage of lung cancer, and quite different from those with onset of symptoms. So it is of importance for the elderly to conduct physical examination that is helpful in detecting early lesions and leaves more choice to the elderly for a more thorough treatment.

One prominent clinical feature of the elderly NSCLC is variety of concurrent diseases, such as diabetes, cardiovascular disease, COPD, and each of these accompanying diseases has a negative impact on the length of survival time. Death caused by other conditions than lung cancer is one key characteristic of the super-aged NSCLC[5]. The degraded physiological functions of the elderly NSCLC patients may work properly under the non-stress state, but once shaken by anesthesia and surgery, they may soon lose

their compensatory ability and result in organ failure. So the dealing with the elderly patients is more difficult than with young patients. Full preoperative preparation plays an important role in securing surgical safety and reducing postoperative complications. Out of 52 cases of super-aged NSCLC patients, 19 cases (36.5%) presented one concomitant disease, 21 cases (42.3%) presented two, 4 cases (7.7%) presented three, and eight cases (15.4%) presented none. The most common concomitant diseases are hypertension, coronary heart disease, and chronic bronchitis. To the smoking patients, besides cessation before operation, respiratory function exercise as well as expectoration and control of airway inflammation by medication should be undertaken. The function of cardiac compensation in the elderly patients is weak, and will be further weakened or disordered by surgical stimulation and the functional changes of endocrine system and immune system. Therefore, polarized liquid can be used to protect myocardium before operation so as to adjust to the best systemic state for operation.

Surgical treatment is the most effective method for early NSCLC and presents an obvious advantage in prolonging the survival time compared with radiotherapy and chemotherapy alone. Sirbu reported the 2-year survival rate of lung cancer patients over 70 years was 6% when they received non-surgical treatment, while it reached 35.6% when they underwent operation[6]. Suemitsu[7] regarded that surgical treatment is an important method for NSCLC among over 80 years, especially for those in early stage. The standard surgical treatment of NSCLC is lobectomy and systematic lymph node dissection. So far there is no surgical method specific for elderly NSCLC patients. What we are using for these patients is by following the general principle of "maximal removal of tumor and maximal retention of normal tissues", lobectomy, lung segment or wedge resection are usually adopted and pneumoectomy or sleeve lobectomy is cautiously considered, after the patients' physical status and organ functions are fully considered. Some researchers reported phase I lung cancer patients older than 80 years can undertake wedge resection of lesion; Pathologically N2 patients aged over 80 should avoid surgery[8]. Mery *et al*[9] found that lobectomy was superior to wedge resection for lung cancer patients under age 65, but showed no significant impact on the long-term survival among patients over 71 years. It is through sub-lobectomy only that the elderly patients with early lung cancer can obtain the similar outcome that lobectomy achieved[10]. Patients in our study underwent anatomical lobectomy and lymph node dissection in 32 cases (65.6%), sub-lobectomy and systematic lymph node sampling in 20 cases (38.4%) [pulmonary wedge resection in 16 cases (30.8%) and lung resection 4 cases (7.7%)]. The postoperative 1-, 3- and 5-year survival rate was 86.0%, 61.8% and 21.5% after lobectomy and 89.0%, 58.3% and 18.7% after sub-lobectomy, without significant difference between lobectomy and sub-lobectomy ($P>0.05$). As long as the patient's

physical conditions permit, radical lung resection should be considered[11]. If the lesions are at early stage and the patients have poor cardiopulmonary function, lung segment resection or wedge resection can be applied and would achieve better results.

The reports on age impact on postoperative complications and mortality of lung cancer vary. Jaklitsch[12] reported the complication rate of 1 020 lung cancer patients ≥ 70 years was 19%–48% and their postoperative mortality was 1%–22%. Schneider[11] reported mortality after lobectomy was closely related to age; the mortality after lobectomy was 0.9% (8/919) among those below 65 years, 1.9% (9/486) among those between 65 to 75 years, and 4.0% (4/100) among those over 75. Zhao[13] reported the postoperative complication rate of 498 lung cancer patients over 70 was 32.7% and the mortality rate was 3.4%. The results from Cerfolid research[14] showed that there were no significant differences in hospital stay days, severe complications and perioperative mortality between those NSCLC patients over 70 and below 70. In the patients of our study, the postoperative complication rate was 44.2% (23/52) and their mortality was 3.8% (2/52). The postoperative complications involving cardiovascular system and respiratory system were related to preoperative diseases, which suggests the importance of active and proper handling of those diseases before operation. Postoperative arrhythmia posed a high incidence, mostly supraventricular tachycardia and atrial fibrillation. Arrhythmia was related to pain from wound, hypovolemia, hypoxia, smoking history, arrhythmia history, postoperative atelectasis, and pulmonary infection. It would effectively reduce the incidence of arrhythmia through oxygen supply during operation, maintenance of stable blood pressure by reducing blood loss, lessening anesthetic and operation time, gentle operation to minimize traction on pulmonary hilus and squeeze on heart.

In conclusion, the surgical risk for the super-aged (over 80) NSCLC patients is acceptable. Age alone is not a surgical contraindication. For those super-aged NSCLC patients, who are in good physical condition, with no serious concomitant diseases and in early stage of lung cancer, should undertake surgical treatment and better outcome can be expected.

Conflict of interest statement

We declare that we have no conflict of interest.

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